

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
29 July 2004 (29.07.2004)

PCT

(10) International Publication Number
WO 2004/062551 A3

(51) International Patent Classification⁷: **C07K 16/36**,
16/18, C12N 15/13, A61K 39/395, 38/49, A61P 7/02,
A61M 31/00

(74) Agents: **BRANTS, Johan, Philippe, Emile et al.**; De
Clercq, Brants & Partners, E. Gevaertdreef 10a, B-9830
Sint-Martens-Latem (BE).

(21) International Application Number:
PCT/BE2004/000002

(22) International Filing Date: 9 January 2004 (09.01.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

03447005.4	10 January 2003 (10.01.2003)	EP
PCT/EP03/06581	23 June 2003 (23.06.2003)	EP
PCT/EP03/07313	8 July 2003 (08.07.2003)	EP
PCT/BE03/00193		
	7 November 2003 (07.11.2003)	BE
PCT/BE03/00189		
	7 November 2003 (07.11.2003)	BE
PCT/BE03/00190		
	7 November 2003 (07.11.2003)	BE
PCT/BE03/00192		
	7 November 2003 (07.11.2003)	BE
PCT/BE03/00194		
	7 November 2003 (07.11.2003)	BE
PCT/BE03/00206		
	1 December 2003 (01.12.2003)	BE
PCT/BE03/00191		
	2 December 2003 (02.12.2003)	BE

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

Published:

— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(71) Applicant (for all designated States except US): **ABLYNX**
N.V. [BE/BE]; Technologiepark 4, B-9052 Zwijnaarde
(BE).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **SILENCE, Karen**
[BE/BE]; Jean Tombeurstraat 21, B-3090 Overijse (BE).

(88) Date of publication of the international search report:
2 September 2004

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: RECOMBINANT VHH SINGLE DOMAIN ANTIBODY FROM CAMELIDAE AGAINST VON WILLEBRAND FAC-
TOR (vWF) OR AGAINST COLLAGEN

(57) Abstract: The present invention relates to polypeptides comprising at least one single domain antibody directed against vWF, vWF A1 domain, A1 domain of activated vWF, vWF A3 domain, gpIb and/or collagen, for the treatment for conditions which require a modulation of platelet-mediated aggregation. A further aspect of the invention is methods of production of said polypeptides, methods to coat devices with such polypeptides used in medical procedures (e.g. PCTA, stenting) and kits for the diagnosis of diseases related to platelet-mediated aggregation.

WO 2004/062551 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE2004/000002

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/36 C07K16/18 C12N15/13 A61K39/395 A61K38/49
A61P7/02 A61M31/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2001/024647 A1 (MCLEOD ANNE ET AL) 27 September 2001 (2001-09-27) paragraph '0013! - paragraph '0025!; claims 1-17	1-28, 30-32
Y	ARBABI GHAHROUDI M ET AL: "SELECTION AND IDENTIFICATION OF SINGLE DOMAIN ANTIBODY FRAGMENTS FROM CAMEL HEAVY-CHAIN ANTIBODIES" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 414, no. 3, 15 September 1997 (1997-09-15), pages 521-526, XP002069903 ISSN: 0014-5793 page 521, right-hand column, paragraphs 4,5 page 525, right-hand column, paragraph 3	1-28, 30-32
-/-		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

9 July 2004

Date of mailing of the international search report

19/07/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Le Flao, K

INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE2004/000002

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2002/028204 A1 (KITO MORIKAZU ET AL) 7 March 2002 (2002-03-07) paragraph '0103! - paragraph '0167!	1-28, 30-32
Y	MUYLDERMANS S: "SINGLE DOMAIN CAMEL ANTIBODIES: CURRENT STATUS" REVIEWS IN MOLECULAR BIOTECHNOLOGY, ELSEVIER, AMSTERDAM,, NL, vol. 74, no. 4, June 2001 (2001-06), pages 277-302, XP001057480 ISSN: 1389-0352 the whole document	1-28, 30-32
Y	US 6 251 393 B1 (MCLEOD ANNE ET AL) 26 June 2001 (2001-06-26) column 3 - column 6	1-28, 30-32
Y	WO 02/057445 A (MURUGANANDAM ARUMUGAM ; STANIMIROVIC DANICA (CA); NARANG SARAM (CA); N) 25 July 2002 (2002-07-25) page 24, line 1 - page 47, line 15	1-28, 30-32
A	CORTEZ-RETAMOZO V ET AL: "Efficient tumor targeting by single-domain antibody fragments of camels" INTERNATIONAL JOURNAL OF CANCER, NEW YORK, NY, US, vol. 98, no. 3, 20 March 2002 (2002-03-20), pages 456-462, XP002248403 ISSN: 0020-7136 page 457, left-hand column, paragraphs 3,4	1-28, 30-32

INTERNATIONAL SEARCH REPORT

International application No.

PCT/BE2004/000002

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purpose of search
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/BE2004/000002

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 29
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 29

Present claim 29 relates to a compound defined by reference to a desirable characteristic or property, namely "that modulates platelet-mediated aggregation identified according to the method of claim 27".

The claims cover any compound having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and no disclosure within the meaning of Article 5 PCT for such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claim also lacks clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, no the search has been carried out for this claim.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/BE2004/000002

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 2001024647	A1	27-09-2001	US 6251393 B1	26-06-2001
			US 2004109858 A1	10-06-2004
			AU 755549 B2	12-12-2002
			AU 1212700 A	15-05-2000
			CA 2344606 A1	04-05-2000
			EP 1124856 A1	22-08-2001
			JP 2002529373 T	10-09-2002
			WO 0024781 A1	04-05-2000
US 2002028204	A1	07-03-2002	AT 236993 T	15-04-2003
			CA 2206423 A1	06-06-1996
			CN 1174575 A	25-02-1998
			DE 69530316 D1	15-05-2003
			DE 69530316 T2	12-02-2004
			DK 795608 T3	21-07-2003
			EP 0795608 A1	17-09-1997
			ES 2197210 T3	01-01-2004
			FI 972279 A	29-07-1997
			WO 9617078 A1	06-06-1996
			JP 3331377 B2	07-10-2002
			NO 972253 A	29-07-1997
			PT 795608 T	29-08-2003
			US 6280731 B1	28-08-2001
			US 5916805 A	29-06-1999
US 6251393	B1	26-06-2001	US 2004109858 A1	10-06-2004
			US 2001024647 A1	27-09-2001
			AU 755549 B2	12-12-2002
			AU 1212700 A	15-05-2000
			CA 2344606 A1	04-05-2000
			EP 1124856 A1	22-08-2001
			JP 2002529373 T	10-09-2002
			WO 0024781 A1	04-05-2000
WO 02057445	A	25-07-2002	AU 6885501 A	03-12-2001
			WO 0190190 A2	29-11-2001
			WO 02057445 A1	25-07-2002
			CA 2380443 A1	29-11-2001
			CA 2441903 A1	25-07-2002
			EP 1328626 A1	23-07-2003
			US 2003190598 A1	09-10-2003